Serial No.: 09/847,670 Confirmation No.: 4815 Filed: May 2, 2001

For: HEPATITIS C VIRUS HELICASE CRYSTALS, CRYSTALLOGRAPHIC STRUCTURE AND METHODS

and dithiothreitol;

concentrating the Hepatitis C virus helicase to a concentration of about 12-16mg/mL; combining concentrated Hepatitis C virus helicase with the ligand in a mixture comprising about 4% by weight to about 14% by weight PEG and about 5% by weight to about 15% by weight DMSO; and

growing a co-crystal by vapor diffusion.

- 33. The method of claim 32 wherein combining the concentrated Hepatitis C virus helicase with the ligand in a mixture comprising PEG and DMSO and growing the co-crystal are performed in the absence of potassium phosphate.
- 34. The method of claim 32 wherein the ligand binds to an NTP binding site on the Hepatitis C virus helicase.
- 35. A method for crystallizing a Hepatitis C virus helicase molecule or molecular complex comprising growing a crystal by vapor diffusion with macro-seeding from a precipitant solution comprising purified Hepatitis C virus helicase, HEPES, and about 4% by weight to about 14% by weight mono-alkyl ether of PEG.
- 36. A method for co-crystallizing a Hepatitis C virus helicase molecule and a ligand to yield a molecular complex, comprising growing a crystal by vapor diffusion with macro-seeding from a precipitant solution comprising purified HCV helicase, HEPES, about 4% by weight to about 14% by weight mono-alkyl ether of PEG, and the ligand, wherein the ligand binds to at least one oligonucleotide binding site on the Hepatitis C virus helicase.
- 37. The method of claims 31-36 wherein the amino acid sequence of the Hepatitis C virus helicase is SEQ ID NO:1.

## Amendment and Response - Appendix A

Serial No.: 09/847,670 Confirmation No.: 4815 Filed: May 2, 2001

For: HEPATITIS C VIRUS HELICASE CRYSTALS, CRYSTALLOGRAPHIC STRUCTURE AND METHODS

Page A-5

- 38. Crystalline Hepatitis C virus helicase comprising a tetragonal crystal having unit cell dimensions of  $a = b = 109 \text{ Å} \pm 3 \text{ Å}$ ;  $c = 84 \text{ Å} \pm 2 \text{ Å}$ ;  $\alpha = \beta = \gamma = 90^{\circ}$ ; and space group P4<sub>1</sub>; the unit cell containing two molecules in an asymmetric unit.
- 39. The crystalline Hepatitis C virus helicase of claim 38 wherein the amino acid sequence of Hepatitis C virus helicase is SEQ ID NO:1.
- 40. Crystalline Hepatitis C virus helicase comprising an orthorhombic crystal characterized by unit cell dimensions of  $a = 66 \text{ Å} \pm 2 \text{ Å}$ ;  $b = 110 \text{ Å} \pm 3 \text{ Å}$ ;  $c = 64 \text{ Å} \pm 2 \text{ Å}$ ;  $\alpha = \beta = \gamma = 90^{\circ}$ ; and a space group P2<sub>1</sub>2<sub>1</sub>2; the unit cell containing one molecule in the asymmetric unit.
- 41. The crystalline Hepatitis C virus helicase of claim 40 wherein the amino acid sequence of Hepatitis C virus helicase is SEQ ID NO:1.
- 42. (Amended) Crystalline Hepatitis C virus helicase having [an] amino acid sequence [is] SEQ ID NO:1.
- 43. A composition comprising crystalline Hepatitis C virus helicase of any of claims 38-42.
- 47. A method for incorporating a chemical entity in a crystal comprising placing a tetragonal crystal of Hepatitis C virus helicase having unit cell dimensions of  $a = b = 109 \text{ Å} \pm 3 \text{ Å}$ ;  $c = 84 \text{ Å} \pm 2 \text{ Å}$ ;  $\alpha = \beta = \gamma = 90^\circ$ ; and space group P4<sub>1</sub> in an aqueous solution comprising about 1mM to about 10mM chemical entity, and 0% by weight to about 15% by weight DMSO.
- 48. A method for incorporating a chemical entity in a crystal comprising placing an orthorhombic crystal of Hepatitis C virus helicase having unit cell dimensions of  $a = 66 \text{ Å} \pm 2 \text{ Å}$ ;  $b = 110 \text{ Å} \pm 3 \text{ Å}$ ;  $c = 64 \text{ Å} \pm 2 \text{ Å}$ ;  $\alpha = \beta = \gamma = 90^\circ$ ; and a space group P2<sub>1</sub>2<sub>1</sub>2 in an aqueous

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solution comprising about 1mM to about 10mM chemical entity, and 0% by weight to about 15% by weight DMSO.

49. **(New)** Crystalline Hepatitis C virus helicase wherein the amino acid sequence of Hepatitis C virus helicase is SEQ ID NO:1.

Page A-6